

WE CLAIM:

1. A glucose biosensor for *in vivo* or *in vitro* use comprising:
at least one mutated binding protein and at least one reporter group attached thereto, such that said reporter group provides a detectable and reversible signal change when said mutated binding protein is exposed to varying glucose concentrations, wherein said detectable and reversible signal change is related to said varying concentrations.
2. The biosensor of claim 1 wherein said mutated binding protein is glucose/galactose binding protein.
3. The biosensor of claim 1 wherein said binding protein comprises at least one amino acid substitution.
4. The biosensor of claim 1 wherein said binding protein comprises at least two amino acid substitutions.
5. The biosensor of claim 1 wherein said binding protein comprises at least three amino acid substitutions.
6. The biosensor of claim 3 wherein said amino acid substitution is selected from the group consisting of a cysteine at position 1, a serine at position 1, a cysteine at position 11, a cysteine at position 14, a cysteine at position 19, a cysteine at position 43, a cysteine at position 74, a cysteine at position 107, a cysteine at position 110, a cysteine at position 112, a cysteine at position 113, a cysteine at position 137, a cysteine at position 149, a cysteine at position 213, a cysteine at position 216, a cysteine at position 238, a cysteine at position 287, and a cysteine at position 292, a cysteine at position 152, a cysteine at position 182, a cysteine at position 236, a cysteine at position 296.
7. The biosensor of claim 6 wherein said binding protein additionally comprises at least one histidine tag.
8. The biosensor of claim 4 wherein said at least two amino acid substitutions are selected from the group consisting of a cysteine at position 112 and a serine at position 238, a cysteine at position 149 and a serine at position 238, a cysteine at position 152 and a cysteine at position 182, a cysteine at position 152 and a serine at position 213, a cysteine at position 213 and a cysteine at position 238, a cysteine at position 149 and an arginine at position 213, a cysteine at

position 149 and a cysteine at position 213, a cysteine at position 149 and a threonine at position 213, a cysteine at position 149 and a leucine at position 213, a cysteine at position 149 and a tyrosine at position 213, a cysteine at position 149 and an asparagine at position 223, a cysteine at position 149 and a cysteine at position 238, a cysteine at position 149 and a serine at position 256, a cysteine at position 149 and an arginine at position 256, a cysteine at position 152 and an arginine at position 213, a cysteine at position 152 and an asparagine at position 223, a cysteine at position 149 and a serine at position 213, and a cysteine at position 213 and a cysteine at position 255.

9. The biosensor of claim 8 wherein said binding protein additionally comprises at least one histidine tag.

10. The biosensor of claim 5 wherein said at least three amino acid substitutions are selected from the group consisting of a cysteine at position 149, a serine at position 213 and a serine at position 238; a cysteine at position 149, an arginine at position 213 and a serine at position 238; a cysteine at position 149, a cysteine at position 213 and a cysteine at position 238; a cysteine at position 149, a serine at position 213 and an asparagine at position 223; a cysteine at position 149, an asparagine at position 223 and an arginine at position 256; a cysteine at position 149, an arginine at position 213 and a cysteine at position 238; and a cysteine at position 149, a cysteine at position 213 and a serine at position 238.

11. The biosensor of claim 10 wherein said binding protein additionally comprises at least one histidine tag.

12. The biosensor of claim 1 having at least four amino acid substitutions.

13. The biosensor of claim 12 wherein said binding protein additionally comprises at least one histidine tag.

14. The biosensor of claim 12 wherein said four amino acid substitutions are selected from the group consisting of a serine at position 1, a cysteine at position 149, an arginine at position 213 and a serine at position 238; a serine at position 1, a cysteine at position 149, a serine at position 213 and a serine at position 238; and a cysteine at position 149, a cysteine at position 182, a cysteine at position 213 and a serine at position 238.

15. The biosensor of claim 14 wherein said four amino acid substitutions are a serine at position 1, a cysteine at position 149, an arginine at position 213 and a serine at position 238.
16. The biosensor of claim 1 wherein said reporter group is a luminescent label.
17. The biosensor of claim 16 wherein said luminescent label has an excitation wavelength of more than about 600 nanometers.
18. The biosensor of claim 16 wherein said luminescent label has an emission wavelength of more than about 600 nanometers.
19. The biosensor of claim 16 wherein said luminescent label is covalently coupled to said at least one glucose/galactose binding protein.
20. The biosensor of claim 19 wherein said luminescent label is covalently coupled to said glucose/galactose binding protein by reaction with at least one member selected from the group consisting of fluorescein, coumarins, rhodamines, 5-TMR1A (tetramethylrhodamine-5-iodoacetamide), (9-(2(or 4)-(N-(2-maleimidyloethyl)-sulfonamidyl)-4(or 2)-sulfophenyl)-2,3,6,7,12,13,16,17-octahydro-(1H,5H,11H,15H-xantheno(2,3,4-ij:5,6,7-i'j')diquinolizin-18-ium salt) (Texas Red®), 2-(5-(1-(6-(N-(2-maleimidyloethyl)-amino)-6-oxohexyl)-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene)-1,3-propyldienyl)-1-ethyl-3,3-dimethyl-5-sulfo-3H-indolium salt (CyTM3), N-((2-iodoacetoxy)ethyl)-N-methylamino-7-nitrobenzoxadiazole (IANBD), 6-acryloyl-2-dimethylaminonaphthalene (acrylodan), pyrene, 6-amino-2,3-dihydro-2-(2-((iodoacetyl)amino)ethyl)-1,3-dioxo-1H-benz(de)isoquinoline-5,8-disulfonic acid salt (lucifer yellow), 2-(5-(1-(6-(N-(2-maleimidyloethyl)-amino)-6-oxohexyl)-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene)-1,3-pentadienyl)-1-ethyl-3,3-dimethyl-5-sulfo-3H-indolium salt (CyTM5), 4-(5-(4-dimethylaminophenyl)oxazol-2-yl)phenyl-N-(2-bromoacetamidoethyl)sulfonamide (Dapoxyl® (2-bromoacetamidoethyl)sulfonamide)), (N-(4,4-difluoro-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-s-indacene-2-yl)iodoacetamide (BODIPY® 507/545 IA), N-(4,4-difluoro-5,7-diphenyl-4-bora-3a,4a-diaza-s-indacene-3-propionyl)-N'-iodoacetylenediamine (BODIPY 530/550 IA), 5-((((2-iodoacetyl)amino)ethyl)amino)naphthalene-1-sulfonic acid (1,5-IAEDANS), and carboxy-X-rhodamine, 5/6-iodoacetamide (XRIA 5,6).

21. The biosensor of claim 1 wherein said reporter group emits said signal in response to exposure to an energy source.
22. A method for glucose detection comprising:
- a) providing at least one mutated glucose/galactose binding protein and at least one reporter group attached thereto;
 - b) exposing said mutated glucose/galactose binding protein to varying glucose concentrations; and
 - c) detecting a detectable and reversible signal change from said reporter group wherein said detectable and reversible signal change corresponds to said varying glucose concentrations.
23. The method of claim 22 wherein said detecting is continuous, programmed, episodic, or combinations thereof.
24. The method of claim 22 wherein said mutated glucose/galactose binding protein is selected from bacterial periplasmic binding proteins.
25. The method of claim 22 wherein said detecting of detectable and reversible signal changes from said reporter group of varying glucose concentrations is *in vivo*.
26. The method of claim 22 wherein said binding protein comprises one amino acid substitution.
27. The method of claim 26 wherein said binding protein comprises at least two amino acid substitutions.
28. The method of claim 27 wherein said binding protein comprises at least three amino acid substitutions.
29. The method of claim 26 wherein said one amino acid substitution is selected from the group consisting of a cysteine at position 1, a serine at position 1, a cysteine at position 11, a cysteine at position 14, a cysteine at position 19, a cysteine at position 43, a cysteine at position 74, a cysteine at position 107, a cysteine at position 110, a cysteine at position 112, a cysteine at position 113, a cysteine at position 137, a cysteine at position 149, a cysteine at position 213, a cysteine at position 216, a cysteine at position 238, a cysteine at position 287, a cysteine at

position 292, a cysteine at position 152, a cysteine at position 182, a cysteine at position 236, and a cysteine at position 296.

30. The method of claim 29 wherein said mutated glucose/galactose binding protein additionally comprises at least one histidine tag.

31. The method of claim 27 wherein said mutated glucose/galactose binding protein has at least two amino acid substitutions selected from the group consisting of a cysteine at position 112 and a serine at position 238, a cysteine at position 149 and a serine at position 238, a cysteine at position 152 and a serine at position 213, a cysteine at position 213 and a cysteine at position 238, a cysteine at position 149 and an arginine at position 213, a cysteine at position 149 and a cysteine at position 213, a cysteine at position 149 and a threonine at position 213, a cysteine at position 149 and a leucine at position 213, a cysteine at position 149 and a tyrosine at position 213, a cysteine at position 149 and a serine at position 213, a cysteine at position 149 and an asparagine at position 223, a cysteine at position 149 and a cysteine at position 238, a cysteine at position 149 and a serine at position 256, a cysteine at position 149 and an arginine at position 256, a cysteine at position 152 and an arginine at position 213, a cysteine at position 152 and an asparagine at position 223, a cysteine at position 213 and a cysteine at position 255.

32. The method of claim 31 wherein said mutated glucose/galactose binding protein additionally comprises at least one histidine tag.

33. The method of claim 28 wherein said glucose/galactose binding protein has at least three amino acid substitutions selected from the group consisting of a cysteine at position 149, a serine at position 213 and a serine at position 238; a cysteine at position 149, an arginine at position 213 and a serine at position 238; a cysteine at position 149, a cysteine at position 213 and a cysteine at position 238; a cysteine at position 149, a serine at position 213 and an asparagine at position 223; a cysteine at position 149, an asparagine at position 223 and an arginine at position 256; a cysteine at position 149, an arginine at position 213 and a cysteine at position 238; and a cysteine at position 149, a cysteine at position 213 and a serine at position 238.

34. The method of claim 33 wherein said mutated glucose/galactose binding protein additionally comprises at least one histidine tag.

35. The method of claim 27 wherein said binding protein comprises at least four amino acid substitutions.
36. The method of claim 35 wherein said four amino acid substitutions are selected from the group consisting of a serine at position 1, a cysteine at position 149, an arginine at position 213 and a serine at position 238; and a cysteine at position 149, a cysteine at position 182, a cysteine at position 213 and a serine at position 238.
37. The method of claim 36 wherein said four amino acid substitutions are a serine at position 1, a cysteine at position 149, an arginine at position 213 and a serine at position 238.
38. The method of claim 22 wherein said reporter group is a luminescent label.
39. The method of claim 38 wherein said luminescent label has an excitation wavelength of more than about 600 nanometers.
40. The method of claim 38 wherein said luminescent label has an emission wavelength of more than about 600 nanometers.
41. The method of claim 38 wherein said luminescent label is covalently coupled to said mutated glucose/galactose binding protein by reacting said mutated binding protein and at least one member selected from the group consisting of fluorescein, coumarins, rhodamines, 5-TMR1A (tetramethylrhodamine-5-iodoacetamide), (9-(2(or4)-(N-(2-maleimidyethyl)-sulfonamidyl)-4(or 2)-sulfophenyl)-2,3,6,7,12,13,16,17-octahydro-(1H,5H,11H,15H-xantheno(2,3,4-ij:5,6,7-i'j')diquinolizin-18-ium salt) (Texas Red®), 2-(5-(1-(6-(N-(2-maleimidyethyl)-amino)-6-oxohexyl)-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene)-1,3-propyldienyl)-1-ethyl-3,3-dimethyl-5-sulfo-3H-indolium salt (CyTM3), N-((2-iodoacetoxy)ethyl)-N-methylamino-7-nitrobenzoxadiazole (IANBD), 6-acryloyl-2-dimethylaminonaphthalene (acrylodan), pyrene, 6-amino-2,3-dihydro-2-(2-((iodoacetyl)amino)ethyl)-1,3-dioxo-1H-benz(de)isoquinoline-5,8-disulfonic acid salt (lucifer yellow), 2-(5-(1-(6-(N-(2-maleimidyethyl)-amino)-6-oxohexyl)-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene)-1,3-pentadienyl)-1-ethyl-3,3-dimethyl-5-sulfo-3H-indolium salt (CyTM5), 4-(5-(4-dimethylaminophenyl)oxazol-2-yl)phenyl-N-(2-bromoacetamidoethyl)sulfonamide (Dapoxyl® (2-bromoacetamidoethyl)sulfonamide)), (N-(4,4-difluoro-1,3,5,7-tetramethyl-4-bora-3a,4a-diazas-indacene-2-yl)iodoacetamide (BODIPY® 507/545 IA), N-(4,4-difluoro-5,7-diphenyl-4-bora-

3a,4a-diaza-*s*-indacene- 3-propionyl)- *N'*-iodoacetylenediamine (BODIPY 530/550 IA), 5-(((2-iodoacetyl)amino)ethyl) amino)naphthalene-1-sulfonic acid (1,5-IAEDANS), and carboxy-X-rhodamine, 5/6- iodoacetamide (XR1A 5,6).

42. The method of claim 22 additionally comprising the step of exposing said reporter group to an energy source capable of exciting said reporter group to emit said signal.

43. A composition comprising:

a mutated glucose/galactose binding protein having at least one amino acid substitution selected from the group consisting of a cysteine at position 1, a serine at position 1, a cysteine at position 11, a cysteine at position 14, a cysteine at position 19, a cysteine at position 43, a cysteine at position 74, a cysteine at position 107, a cysteine at position 110, a cysteine at position 112, a cysteine at position 113, a cysteine at position 137, a cysteine at position 149, a cysteine at position 213, a cysteine at position 216, a cysteine at position 238, a cysteine at position 287, a cysteine at position 292, a cysteine at position 236, and a cysteine at position 296.

44. The composition of claim 43 wherein said mutated glucose/galactose binding protein additionally comprises at least one histidine tag.

45. The composition of claim 43 wherein said mutated glucose/galactose binding protein additionally comprises at least one reporter group.

46. The composition of claim 45 wherein at least one reporter group is a luminescent label.

47. The composition of claim 46 wherein said luminescent label has an excitation wavelength of more than about 600 nanometers.

48. The composition of claim 46 wherein said luminescent label has an emission wavelength of more than about 600 nanometers.

49. The composition of claim 46 wherein said luminescent label is covalently coupled to said mutated glucose/galactose binding protein by reacting said mutated binding protein and at least one member selected from the group consisting of fluorescein, coumarins, rhodamines, 5-TMR1A (tetramethylrhodamine-5-iodoacetamide), (9-(2(or4)-(N-(2-maleimidyethyl)-sulfonamidyl)-4(or 2)-sulfophenyl)-2,3,6,7,12,13,16,17-octahydro-(1H,5H,11H,15H-xantheno(2,3,4-ij:5,6,7-i'j')diquinolizin-18-ium salt) (Texas Red®), 2-(5-(1-(6-(N-(2-maleimidyethyl)-amino)-6-oxohexyl)-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene)-1,3-

propyldienyl)-1-ethyl-3,3-dimethyl-5-sulfo-3H-indolium salt (CyTM3), N-((2-iodoacetoxy)ethyl)-N-methylamino-7-nitrobenzoxadiazole (IANBD), 6-acryloyl-2-dimethylaminonaphthalene (acrylodan), pyrene, 6-amino-2,3-dihydro-2-(2-((iodoacetyl)amino)ethyl)-1,3-dioxo-1H-benz(de)isoquinoline-5,8-disulfonic acid salt (lucifer yellow), 2-(5-(1-(6-(N-(2-maleimidyethyl)-amino)-6-oxohexyl)-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene)-1,3-pentadienyl)-1-ethyl-3,3-dimethyl-5-sulfo-3H-indolium salt (CyTM5), 4-(5-(4-dimethylaminophenyl)oxazol-2-yl)phenyl-N-(2-bromoacetamidoethyl)sulfonamide (Dapoxyl® (2-bromoacetamidoethyl)sulfonamide)), (N-(4,4-difluoro-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-s-indacene-2-yl)iodoacetamide (BODIPY® 507/545 IA), N-(4,4-difluoro-5,7-diphenyl-4-bora-3a,4a-diaza-s-indacene-3-propionyl)-N'-iodoacetylenediamine (BODIPY 530/550 IA), 5-(((2-iodoacetyl)amino)ethyl)amino)naphthalene-1-sulfonic acid (1,5-IAEDANS), and carboxy-X-rhodamine, 5/6-iodoacetamide (XRIA 5,6).

50. A composition comprising: a mutated glucose/galactose binding protein having at least one amino acid substitution selected from the group consisting of a cysteine at position 152 and a cysteine at position 182, and at least one additional insertion, deletion or substitution of an amino acid residue.

51. The composition of claim 50 wherein said mutated glucose/galactose binding protein additionally comprises at least one histidine tag.

52. The composition of claim 50 wherein said mutated glucose/galactose binding protein additionally comprises at least one reporter group.

53. The composition of claim 52 wherein at least one reporter group is a luminescent label.

54. The composition of claim 53 wherein said luminescent label has an excitation wavelength of more than about 600 nanometers.

55. The composition of claim 53 wherein said luminescent label has an emission wavelength of more than about 600 nanometers.

56. The composition of claim 53 wherein said luminescent label is covalently coupled to said mutated glucose/galactose binding protein by reacting said mutated binding protein and at least one member selected from the group consisting of fluorescein, coumarins, rhodamines, 5-TMRIA (tetramethylrhodamine-5-iodoacetamide), (9-(2(or4)-(N-(2-maleimidyethyl)-

sulfonamidyl)-4(or 2)-sulfophenyl)-2,3,6,7,12,13,16,17-octahydro-(1H,5H,11H,15H-xantheno(2,3,4-ij:5,6,7-i'j')diquinolizin-18-ium salt) (Texas Red®), 2-(5-(1-(6-(N-(2-maleimidyethyl)-amino)-6-oxohexyl)-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene)-1,3-propyldienyl)-1-ethyl-3,3-dimethyl-5-sulfo-3H-indolium salt (CyTM3), N-((2-iodoacetoxy)ethyl)-N-methylamino-7-nitrobenzoxadiazole (IANBD), 6-acryloyl-2-dimethylaminonaphthalene (acrylodan), pyrene, 6-amino-2,3-dihydro-2-(2-((iodoacetyl)amino)ethyl)-1,3-dioxo-1H-benz(de)isoquinoline-5,8-disulfonic acid salt (lucifer yellow), 2-(5-(1-(6-(N-(2-maleimidyethyl)-amino)-6-oxohexyl)-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene)-1,3-pentadienyl)-1-ethyl-3,3-dimethyl-5-sulfo-3H-indolium salt (CyTM5), 4-(5-(4-dimethylaminophenyl)oxazol-2-yl)phenyl-N-(2-bromoacetamidoethyl)sulfonamide (Dapoxyl® (2-bromoacetamidoethyl)sulfonamide)), (N-(4,4-difluoro-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-s-indacene-2-yl)iodoacetamide (BODIPY® 507/545 IA), N-(4,4-difluoro-5,7-diphenyl-4-bora-3a,4a-diaza-s-indacene-3-propionyl)-N'-iodoacetylenediamine (BODIPY 530/550 IA), 5-(((2-iodoacetyl)amino)ethyl)amino)naphthalene-1-sulfonic acid (1,5-IAEDANS), and carboxy-X-rhodamine, 5/6-iodoacetamide (XRIA 5,6).

57. A composition comprising:

a mutated glucose/galactose binding protein having at least two amino acid substitutions selected from the group consisting of a cysteine at position 112 and a serine at position 238, a cysteine at position 149 and a serine at position 238, a cysteine at position 152 and a serine at position 213, a cysteine at position 213 and a cysteine at position 238, a cysteine at position 149 and an arginine at position 213, a cysteine at position 149 and a cysteine at position 213, a cysteine at position 149 and a threonine at position 213, a cysteine at position 149 and a leucine at position 213, a cysteine at position 149 and a tyrosine at position 213, a cysteine at position 149 and a serine at position 213, a cysteine at position 149 and an asparagine at position 223, a cysteine at position 149 and a cysteine at position 238, a cysteine at position 149 and a serine at position 256, a cysteine at position 149 and an arginine at position 256, a cysteine at position 152 and an arginine at position 213, a cysteine at position 152 and an asparagine at position 223, a cysteine at position 213 and a cysteine at position 255.

58. The composition of claim 57 wherein said mutated glucose/galactose binding protein additionally comprises at least one histidine tag.

59. The composition of claim 57 wherein said mutated glucose/galactose binding protein additionally comprises at least one reporter group.
60. The composition of claim 59 wherein said reporter group is a luminescent label.
61. The composition of claim 60 wherein said luminescent label has an excitation wavelength of more than about 600 nanometers.
62. The composition of claim 60 wherein said luminescent label has an emission wavelength of more than about 600 nanometers.
63. The composition of claim 60 wherein said luminescent label is covalently coupled to said mutated glucose/galactose binding protein by reacting said mutated binding protein and at least one member selected from the group consisting of fluorescein, coumarins, rhodamines, 5-TMR1A (tetramethylrhodamine-5-iodoacetamide), (9-(2(or4)-(N-(2-maleimidyethyl)-sulfonamidyl)-4(or 2)-sulfophenyl)-2,3,6,7,12,13,16,17-octahydro-(1H,5H,11H,15H-xantheno(2,3,4-ij:5,6,7-ij')diquinolizin-18-ium salt) (Texas Red®), 2-(5-(1-(6-(N-(2-maleimidyethyl)-amino)-6-oxohexyl)-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene)-1,3-propyldienyl)-1-ethyl-3,3-dimethyl-5-sulfo-3H-indolium salt (CyTM3), N-((2-iodoacetoxy)ethyl)-N-methyl)amino-7-nitrobenzoxadiazole (IANBD), 6-acryloyl-2-dimethylaminonaphthalene (acrylodan), pyrene, 6-amino-2,3-dihydro-2-(2-((iodoacetyl)amino)ethyl)-1,3-dioxo-1H-benz(de)isoquinoline-5,8-disulfonic acid salt (lucifer yellow), 2-(5-(1-(6-(N-(2-maleimidyethyl)-amino)-6-oxohexyl)-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene)-1,3-pentadienyl)-1-ethyl-3,3-dimethyl-5-sulfo-3H-indolium salt (CyTM5), 4-(5-(4-dimethylaminophenyl)oxazol-2-yl)phenyl-N- (2-bromoacetamidoethyl)sulfonamide (Dapoxyl® (2-bromoacetamidoethyl)sulfonamide)), (N- (4,4-difluoro-1,3,5,7-tetramethyl- 4-bora-3a,4a-diaza-s-indacene- 2-yl)iodoacetamide (BODIPY® 507/545 IA), N-(4,4-difluoro-5,7-diphenyl- 4-bora-3a,4a-diaza-s-indacene- 3-propionyl)- N'-iodoacetylenediamine (BODIPY 530/550 IA), 5-(((2-iodoacetyl)amino)ethyl) amino)naphthalene-1-sulfonic acid (1,5-IAEDANS), and carboxy-X-rhodamine, 5/6- iodoacetamide (XRIA 5,6).
64. A composition comprising:
a mutated glucose/galactose binding protein having at least three amino acid substitutions selected from the group consisting of a cysteine at position 149, a serine at position 213 and a

serine at position 238; a cysteine at position 149, an arginine at position 213 and a serine at position 238; a cysteine at position 149, a cysteine at position 213 and a cysteine at position 238; a cysteine at position 149, a serine at position 213 and an asparagine at position 223; a cysteine at position 149, an asparagine at position 223 and an arginine at position 256; a cysteine at position 149, an arginine at position 213 and a cysteine at position 238; and a cysteine at position 149, a cysteine at position 213 and a serine at position 238.

65. The composition of claim 64 wherein said mutated glucose/galactose binding protein additionally comprises at least one histidine tag.

66. The composition of claim 64 wherein said mutated glucose/galactose binding protein additionally comprises at least one reporter group.

67. The composition of claim 66 wherein said reporter group is a luminescent label.

68. The composition of claim 67 wherein said luminescent label has an excitation wavelength of more than about 600 nanometers.

69. The composition of claim 67 wherein said luminescent label has an emission wavelength of more than about 600 nanometers.

70. The composition of claim 67 wherein said luminescent label is covalently coupled to said mutated glucose/galactose binding protein by reacting said mutated binding protein and at least one member selected from the group consisting of fluorescein, coumarins, rhodamines, 5-TMR1A (tetramethylrhodamine-5-iodoacetamide), (9-(2(or4)-(N-(2-maleimidyethyl)-sulfonamidyl)-4(or 2)-sulfophenyl)-2,3,6,7,12,13,16,17-octahydro-(1H,5H,11H,15H-xantheno(2,3,4-ij:5,6,7-i'j')diquinolizin-18-ium salt) (Texas Red®), 2-(5-(1-(6-(N-(2-maleimidyethyl)-amino)-6-oxohexyl)-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene)-1,3-propyldienyl)-1-ethyl-3,3-dimethyl-5-sulfo-3H-indolium salt (CyTM3), N-((2-iodoacetoxy)ethyl)-N-methyl)amino-7-nitrobenzoxadiazole (IANBD), 6-acryloyl-2-dimethylaminonaphthalene (acrylodan), pyrene, 6-amino-2,3-dihydro-2-(2-((iodoacetyl)amino)ethyl)-1,3-dioxo-1H-benz(de)isoquinoline-5,8-disulfonic acid salt (lucifer yellow), 2-(5-(1-(6-(N-(2-maleimidyethyl)-amino)-6-oxohexyl)-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene)-1,3-pentadienyl)-1-ethyl-3,3-dimethyl-5-sulfo-3H-indolium salt (CyTM5), 4-(5-(4-dimethylaminophenyl)oxazol-2-yl)phenyl-N-(2-bromoacetamidoethyl)sulfonamide (Dapoxyl® (2-

bromoacetamidoethyl)sulfonamide)), (*N*-(4,4-difluoro-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-*s*-indacene-2-yl)iodoacetamide (BODIPY® 507/545 IA), *N*-(4,4-difluoro-5,7-diphenyl-4-bora-3a,4a-diaza-*s*-indacene-3-propionyl)-*N'*-iodoacetylenediamine (BODIPY 530/550 IA), 5-(((2-iodoacetyl)amino)ethyl)amino)naphthalene-1-sulfonic acid (1,5-IAEDANS), and carboxy-X-rhodamine, 5/6-iodoacetamide (XRIA 5,6).

71. A composition comprising:

a mutated glucose/galactose binding protein having at least four amino acid substitutions selected from the group consisting of a serine at position 1, a cysteine at position 149, an arginine at position 213 and a serine at position 238; a serine at position 1, a cysteine at position 149, a serine at position 213 and a serine at position 238; and a cysteine at position 149, a cysteine at position 182, a cysteine at position 213 and a serine at position 238.

72. The composition of claim 71 wherein said mutated glucose/galactose binding protein additionally comprises at least one histidine tag.

73. The composition of claim 71 wherein said mutated glucose/galactose binding protein additionally comprises at least one reporter group.

74. The composition of claim 73 wherein said reporter group is a luminescent label.

75. The composition of claim 74 wherein said luminescent label has an excitation wavelength of more than about 600 nanometers.

76. The composition of claim 74 wherein said luminescent label has an emission wavelength of more than about 600 nanometers.

77. The composition of claim 74 wherein said luminescent label is covalently coupled to said at least one glucose/galactose binding protein by reaction with said at least one mutated binding protein and a member selected from the group consisting of fluorescein, coumarins, rhodamines, 5-TMRIA (tetramethylrhodamine-5-iodoacetamide), (9-(2(or4)-(N-(2-maleimidyethyl)sulfonamidyl)-4(or 2)-sulfophenyl)-2,3,6,7,12,13,16,17-octahydro-(1H,5H,11H,15H-xantheno(2,3,4-ij:5,6,7-ij')diquinolizin-18-ium salt) (Texas Red®), 2-(5-(1-(6-(N-(2-maleimidyethyl)-amino)-6-oxohexyl)-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene)-1,3-propyldienyl)-1-ethyl-3,3-dimethyl-5-sulfo-3H-indolium salt (Cy™3), N-((2-iodoacetoxy)ethyl)-N-methylamino-7-nitrobenzoxadiazole (IANBD), 6-acryloyl-2-dimethylaminonaphthalene

(acrylodan), pyrene, 6-amino-2,3-dihydro-2-(2-((iodoacetyl)amino)ethyl)-1,3-dioxo-1H-benz(de)isoquinoline-5,8-disulfonic acid salt (lucifer yellow), 2-(5-(1-(6-(N-(2-maleimidyethyl)-amino)-6-oxohexyl)-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene)-1,3-pentadienyl)-1-ethyl-3,3-dimethyl-5-sulfo-3H-indolium salt (CyTM5), 4-(5-(4-dimethylaminophenyl)oxazol-2-yl)phenyl-N-(2-bromoacetamidoethyl)sulfonamide (Dapoxyl® (2-bromoacetamidoethyl)sulfonamide)), (*N*-(4,4-difluoro-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-*s*-indacene-2-yl)iodoacetamide (BODIPY® 507/545 IA), *N*-(4,4-difluoro-5,7-diphenyl-4-bora-3a,4a-diaza-*s*-indacene-3-propionyl)-*N*'-iodoacetylenediamine (BODIPY 530/550 IA), 5-(((2-iodoacetyl)amino)ethyl)amino)naphthalene-1-sulfonic acid (1,5-IAEDANS), and carboxy-X-rhodamine, 5/6-iodoacetamide (XRIA 5,6).